Replay to Transesophageal Echocardiography in Patients with Recent Stroke and Normal Carotid Arteries

Response to "Heparin/PF4 antibodies formation after heparin treatment: Temporal aspects and long-term follow-up"

We wish to thank Dr Selleng and coauthors for the interest in our work. They have raised some interesting issues that we comment on, point-by-point, as follows:

Dr Selleng and coauthors are correct: the 4T score we present was calculated from the data at day 30 after surgery (time 2), and therefore, it included all new thrombotic events that occurred within that period. We concur with Dr Selleng that this may have contributed to 4T score being rather high in our study. We wish to point out that this was not part of the initial evaluation of patients, but it was done retrospectively, in response to a specific request by one of the reviewers.

We appreciate that statistical methodology can make a difference. In this respect, we wish to reassure Dr Selleng and all readers of the Journal that data in Table 2 were *not* subjected to Fisher test, but they were actually compared by using the McNemar χ^2 test, which yielded significant differences. This was specified in the Methods section of our article (page 590, lines 7-8 of the "Statistical Analysis" section).[1] As for the choice of McNemar χ^2 test for comparing proportions, this approach has been used in other similar cases.[2]

Finally, we wish to discuss the implications of our study, in light of the comments raised by Selleng et al. However, we first wish to point out that in their letter, Selleng et al, summarize into one sentence what is actually the result of a rather articulate series of statements we made, and therefore the "take home" message may sound different from what we actually meant. Specifically, we concluded that:

"Persistence of heparin-induced antibodies in a substantial number of patients after an initial exposure to UFH suggests that it would be prudent to limit or avoid the use of heparin in patients with known history of HIT." (page 594, lines 27-30). We are confident that there should be no question that in patients with *known history of HIT*, rechallenge with UFH ought to be done with utmost circumspection, or not at all.

The statement "Recommendations for potential alternative anticoagulant therapies among cardiac surgery patients are based on direct thrombin inhibitors" (page 594, lines 31-33) should then be taken as a logical consequence of what said above; that is, if UFH cannot be administered, one should consider alternate thrombin inhibitors. We believe this concept is also widely recognized and apologize if it somehow went distorted.

Finally, we wrote "Moreover, the high prevalence of seropositivity before CABG observed in this study suggests that it might be advisable to prospectively screen for positivity all patients scheduled for elective cardiac surgery, and be on the lookout for possible HIT related events in this population" (page 594, lines 33-38). We honestly think that, given the high incidence of antibody formation, and its potentially relevant clinical consequences, being "on the look out" in CABG patients can be of benefit in the management of these patients.

As for the idea to screen patients scheduled for CABG, we feel that as phrased in the sentence above, this is just as a rather loose suggestion for possible management; indeed, we entirely concur with Dr Selleng's call for prospective randomized trials to specifically address this issue.

We hope that, as an effect of these further clarifications, our findings may be clearer to the readers of the Journal. We wish to thank Selleng et al, and the editors, for the opportunity to provide this further contribution to an important clinical issue.

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2. Williams RT, Damaraju LV, Mascelli MA, et al. Anti-platelet factor 4/heparin antibodies: an independent predictor of 30-day myocardial infarction after acute coronary ischemic syndromes. Circulation 2003; 107:2307-12.